



IN THE UNITED STATES PATENT AND TRADEMARK OFFICE
BEFORE THE BOARD OF PATENT APPEALS AND INTERFERENCES

IN RE: YODER, et al.)
)
) APPEAL NO. _____
 SERIAL NO: 09/772,603)
)
)
 FOR: ISOLATED BOVINE IgG HEAVY)
 CHAIN PROTEIN AND ITS USE)
 AS AN ANTIMICROBIAL) REPLY BRIEF
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 FILED: January 30, 2001)
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 GROUP ART UNIT: 1644)

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To the Commissioner of Patents and Trademarks
Washington, D.C. 20231

Dear Sirs:

Appellants respectfully request that the following Reply Brief be entered into the record. It addresses new arguments set forth in the Examiner's Answer.

I. Introduction

As a preliminary matter, Appellant acknowledges the Examiner's withdrawal of the rejections of claim 8 under 35 U.S.C. 112, second paragraph. In view of this, the only remaining rejection in the case is of claims 8-10 as being unpatentable over U.S. Pat. No. 6,096,310 ("Bier '310") or U.S. Pat. No. 5,871,731 ("Sprotte '731") each in view of Kempf et al. (Transfusion 31(5): 423-27; 1991) under 35 U.S.C. § 103(a).

II. **The Examiner has Failed to Provide the Requisite Motivation for a Person Skilled in the Art to Combine the Teachings of Bier or Sprotte with Kempf**

As noted in Appellant's brief, the Examiner must demonstrate a motivation or suggestion in the prior art as a whole to suggest combining the teachings of the cited prior art references. In re Fine, 837 F.2d 1071, 1074 (Fed. Cir. 1988). In this case, the Examiner has failed to do so and, thus, the rejection for obviousness must be reversed.

A. **Kempf's Teachings Relate Only to Intravenous Immunoglobulin Preparations**

Here, the Examiner has cited the Bier and Sprotte for their alleged teachings of orally administering purified immunoglobulin to mammals for treating gastrointestinal bacterial overgrowth (Bier) and chronic pain syndrome (Sprotte). The Examiner, however, has admitted that the immunoglobulins of Bier and Sprotte are whole and intact, and therefore do not teach oral administration of an acid hydrolyzed, heated, and neutralized IgG fraction, as required by claims 8-10:

The claimed invention as recited in claims 8 differs from the reference only by the recitation of said isolated IgG fraction which is acid hydrolyzed, and has been heat treated from 15 minutes to one hour at a temperature of 35°C to 40°C and thereafter neutralized.

(Paper No. 8, p. 4, para. 4).

The Examiner cited Kempf et al. for the missing teachings of Bier and Sprotte, i.e. administration of IgG that is treated so it no longer whole and intact. However, Kempf teaches the use of his method only in conjunction with the preparation of "immunoglobulin preparations intended for intravenous use (IVIG)" for the purpose of preventing "transmission of non-A, non-B hepatitis (hepatitis C)." (Page 423, first column)(Emphasis supplied).

The Examiner acknowledges that Kempf differs from the claimed invention in that the claimed invention teaches administration of IgG orally to provide bacterial and viral static activity in a mammal. Thus, since Kempf does not suggest applying its methods to orally administered IgG, the requisite motivation for combining the teachings of Kempf with that of Bier and Sprotte is missing.

The Examiner argues that it would have been obvious to one of ordinary skill in the art at the time the invention was made to inactivate and test the bioactivity of virus growth in any IgG preparation by treating any IgG preparation (i.e. oral or I.V.) with acid hydrolysis such as HCl, heated at 37°C for one hour and then neutralized with NaOH as taught by Kempf in the IgG preparation employed by Bier or Sprotte. (Examiner's Brief p. 6). However, the Examiner provides no basis for this conclusion other than a general discussion of the individual teachings of the references. What is missing from the Examiner's conclusion is any reasoning, either explicit or implicit in the references, for a person skilled in the art to combine the teachings of Kempf relating to I.V. immunoglobulin preparations with the oral immunoglobulin preparations of Bier or Sprotte.

In response to Appellant's argument that Kempf provides no incentive to use its teachings in the preparation of an orally administered IgG dosage form as required by claims 8-10, the Examiner argues that Kempf and the FDA have "clearly established" that "viruses such as hepatitis B and C may be present in the plasma (see page 423, column 1 in particular) and any immunoglobulin preparation for therapeutic use clearly has the potential risk of viral transmission (See page 423, column 1, in particular). (Examiner's Brief p. 6). It is not understood, however, how the Examiner can make this assertion since Kempf, and its statements relating to the FDA, while extensively discussing the potential risks with respect to intravenous dosage forms, make no reference whatsoever to oral IgG preparations and their

potential risks and hazards. For this reason, a person skilled in the art would reasonably presume that the same risks are not applicable to oral IgG dosage forms. Otherwise, why would Kempf deliberately limit its discussions to intravenous immunoglobulin dosage forms and not extend them to include all routes of administration?

B. There is No Evidence of Record that Transmission of VSV is of Concern with Any Route of Immunoglobulin Administration Other Than Intravenous

The Examiner also asserts that Kempf teaches that acid hydrolyzed IgG fraction has viral static activity toward viruses "such as Vesicular stomatitis viruses (VSV) which is known to transmit orally and causes foot and mouth disease in live-stocks." (Examiner's Brief, p. 8). This statement by the Examiner is wrong on several counts. First, Kempf does not teach inactivation of VSV in the absence of pepsin, contrary to the claimed invention. (See p. 424 under Results, "...all viruses except VSV were totally inactivated after incubation at pH 4 with or without pepsin.")(Emphasis supplied).

Further, the Examiner provides no basis for the assertion that VSV is known to be transmitted through oral administration of IgG. Certainly the cited references do not support the Examiner's conclusion. Instead, since VSV is grouped with the other intravenously transmitted viruses HIV, hepatitis B and HCV, a person skilled in the art would more reasonably conclude that VSV is problematic only in terms of intravenous administration.

C. Inclusion of Kempf's Viral Inactivation Methods with Bier's Oral Immunoglobulin Preparations Would Serve No Useful Purpose

Finally, in response to Appellant's argument that Bier teaches away from its combination with Kempf on the basis that it uses immunoglobulin from animals that do not carry the disease vectors that are of concern in Kempf, the Examiner argues that Bier would still be inclined to use Kempf's viral inactivation methods on the basis that:

...animal antibodies still have the potential of carrying other animal viruses because it is also fairly assumed that these animals have been exposed over their lifetime to the same range of potential pathogens as human patients.

Examiner's Brief, page 9, second paragraph. This statement by the Examiner, however, is taken entirely out of context. Further, the conclusions drawn from this statement by the Examiner directly contradict Bier's own teachings.

Bier states there are "numerous" advantages to using animal derived immunoglobulins, such as those from cow, sheep, goat, pig or horse. (Col. 2, lines 46-49). First, animal immunoglobulins are more readily accessible and less costly. (Col. 2, lines 49-50). Second, Bier notes that animal immunoglobulins are "far safer" than human immunoglobulins, since "human donors are potential carriers of very serious disease vectors, including hepatitis and HIV", and that even the best screening tactics for human donor blood "cannot guarantee absence of these vectors." (Col. 2, lines 49-55). To the contrary, "animals, such as cows, horses, pigs, sheep and goats, do not carry any of these viral human disease vectors." (Col. 2, lines 55-57)(Emphasis supplied). Thus, Bier concludes that human immunoglobulins, even from well-screened blood, are impractical and unsuitable for use in immunoglobulin preparations, and therefore teaches away from their use.

The sentence taken out of context by the Examiner is Bier's statement that it can be fairly assumed that the animals from which the immunoglobulins are derived "have been exposed over their lifetime to the same range of potential pathogens as human patients and have therefore built up the requisite reservoir of antibodies." (Col. 2, lines 57-60). Upon a complete reading of Bier, however, it is clear that Bier makes this statement for the purpose of showing that animal immunoglobulins would be expected to provide the same beneficial

effects of treating disease in humans as human immunoglobulins since both humans and animals would develop the same antibodies to various diseases over their lifetimes, not that animal immunoglobulins are as hazardous as human immunoglobulins (as the Examiner would have the Board believe). (Col. 2, lines 57-65).

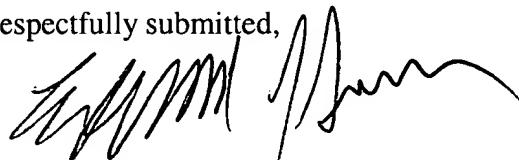
For these reasons, a person skilled in the art would not have any motivation to use the viral inactivation methods of Kempf et al. in combination with the animal immunoglobulins of Bier since the Bier animal immunoglobulins are already free of the human pathogens that are of primary concern in Kempf.

III. Conclusion

Therefore, for the above-stated reasons, and for the reasons set forth in Appellants' appeal brief, Appellants respectfully request reversal of the decision of the Examiner, and allowance of the application.

It is not believed a fee is due with this brief. If a fee is due, please consider this a request to debit or credit Deposit Account No. 26-0084 accordingly.

Respectfully submitted,



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CERTIFICATE OF SERVICE

I hereby certify that a true and correct copy of the foregoing was mailed by First Class Mail, postage prepaid, the 28 day of February, 2003, to Commissioner of Patents and Trademarks, Washington D.C. 20231.



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